U.S.

Williams, Anna Harris 1951 Degeneration and regeneration of antibiotic-producing strains of Streptomyces griseus (Krainsky) Waksman & Henrici. M.S. Thesis U of W.

Yeast glucose agar Y. Ex. 10 Glu 5 K_2HPO_4 1 Agar 15
tap water

Maltose (or starch) Spor. Agar (pH 6.8-7)

Maltose	10
Tryptone	5
K_2HPO_4	.5
NaCl	.5
$FeSO_4$	.1
Agar	20
~~H_2O~~	

more stable. Sporogenesis restored on this medium.

S. griseus references + media:

			B13	
B21	Glucose g.	10	20	~~B22 20~~
	$(NH_4)_2HPO_4$	4		
	$CaCl_2$	.4		
	K_2HPO_4	2	2	See Dulaney et al. Mycologia 1949
	$MgSO_4 \cdot 7$	1	1	Savage J Bact 57:429
	NaCl	5		
				Carvajal Mycologia 1948-9
	$FeSO_4 \cdot 7$ mg	20	10	Kelner J Bact 56:157
	$ZnSO_4 \cdot 7$	10	10	57:73
	add alkali to		Cu 5	
	pH 7		Mn 5	
	Sod lact		8	Waksman: Streptomyces
	NH_4NO_3		2.5	
	$CaCO_3$		1	

Spore suspensions:

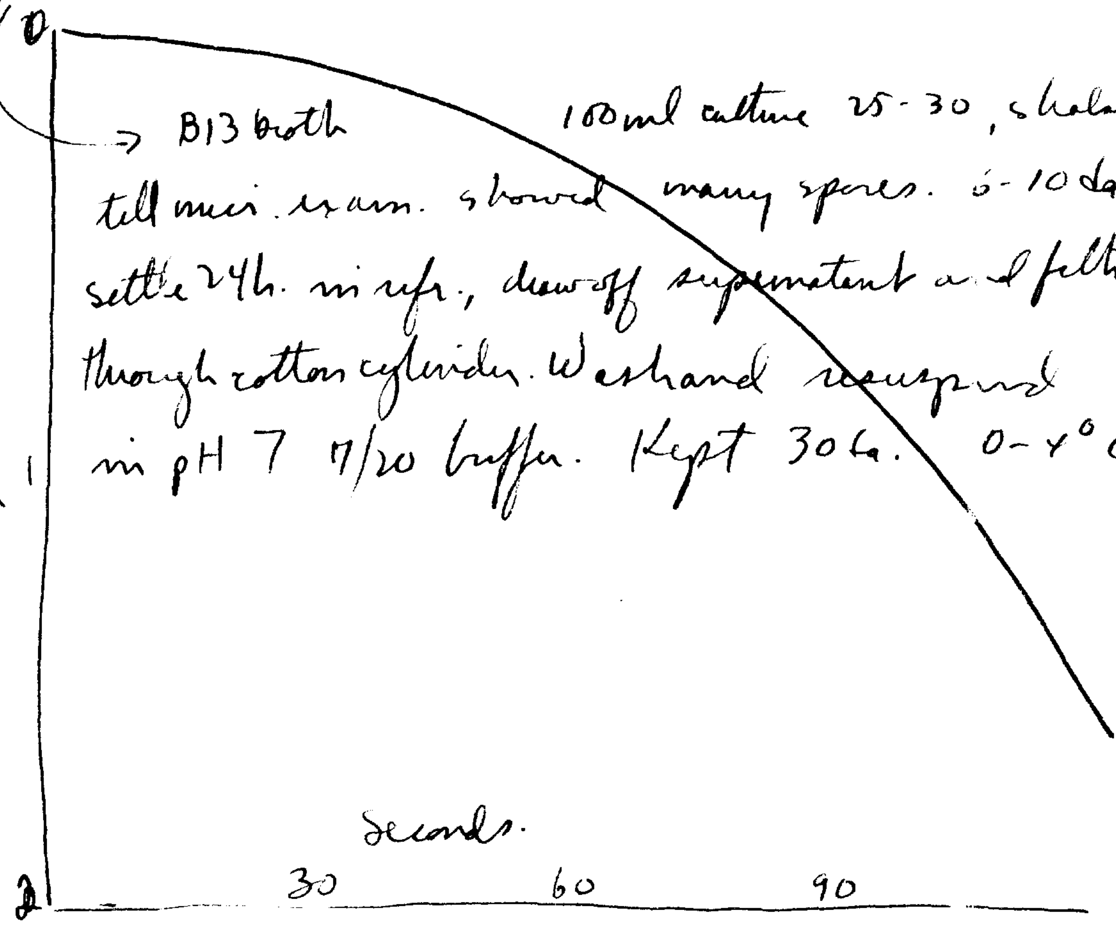
Aerial potato dextrose agar 7-10 days 30°. 5 ml H_2O, gently shaken. suspensions shaken with 10 g. "glow beads". (480 c.p.m. 2 min) diluted with Aerosol OT to give 1:1000. Filter aseptically through cotton.

Submerged → B13 broth 100 ml culture 25-30, shaken till micr. exam. showed many spores. 6-10 da. settle 24 h. in refr., draw off supernatant and filter through cotton cylinder. Wash and resuspend in pH 7 M/20 buffer. Kept 30 da. 0-4°C.

UV - p S.

45 cm

Sterling



Williams Smith, H. (1948) Investigations on the typing of staphylococci by means of bacteriophage I. The origin and nature of lysogenic strains. J. Hyg. 46. 74-81.

A number of coagulase +, $\varphi 42D^{S}$, strains were studied. Many were mutually lysogenic. 7/23 were lysogenic for the other 16., and sometimes mutually. None of these $42D^{S}$ types were λ for other strains. Presence of λ did not necessarily confer mercury-resistance. Very few resistants were non-lysogenic.

Williams Smith, H. (1948) II. The significance of lysogenic strains in staphylococcal type designation. J. Hyg. 46: 82-89.

a) Mixture of $a(\lambda_1) + b(\lambda_2)$ led to the production of new phage types, $c\,a(\lambda_1 \lambda_2)$. A genetic classification was attempted with limited success. Much of the resistance pattern depends on the λ carried.

IL

Cowles, P.B. (1931) J. Bact 22: 119-123. The recovery of bacteriophage from filtrates devoid from heated spore suspensions.

1. B. anthracis. Induced λ. Filtrates from cultures heated to 90° 10 mins were λ; 95° survivors were not, at least from isolated colonies

2. B megatherium 899 (de Jong) Spores survived 90°, and "all colonies .... showed ... bacteriophage"

3. B subtilis (d'Herelle) survived 90° 10m. or 100° 5 mins. Some, but not all, of the spores carried λ.

75° 10 mins. inactivated all the five phages used.

Regards as evidence against spont. generation of φ.

S.A. 20:15-23; 21:161

Flu,P.C., (1938). Etude sur la bacteriophage du Bacterium megatherium. Ann inst Past 60, 610-632.

From summary: Used de Jong's 899 as lysogenic; 338 as indicator.

a) found less phage than bacteria, in contrast to Wollmans

b) very young cultures carry phage alsp, but saline destroys the phage and prevents its filtrability.

Wollman,E. and Wollman,E., (1938) Recherches sur le phenomene de Twort-d'Herelle. V. (Bacteriophagie ou autolyse heredo-contangieuse). Ann inst Past 60, 13-57.

lysogen. megaterium. have sol. bacteriocin

phage ca = bacteria argue that phage particles exist as such in bacteria

phage sensitive at division

not compatible i parasite L'existence de "phages" de la fonction lysogène et la production de novo des particules corpusculeuses bactériophages paraissant démontrer l'origine endogène de ceux-ci

Phage
Summary.

Burnet,F.M. & McKie,M. (1929). Observations on a permanently lysogenic strain of B. enteritidis Gaertner. AJMS 6:276-284.

Lysogenicity determined by growing test strain with indicator, heating to 56 for 30 mins to kill bacteria and plating on indicator for plaques. Titers of 10^7 - 10^8 often obtained in most isolates; others showed 10^3-10^4.

Repeated washing continued to liberate phage. After almost exhaustive washing with saline, distilled water liberated additional large quantities of phage. Lysis by other phages diminished the yield.

Lysogenicity was found to be permanent ' "The permanence of the lysogenic character makes it necessary to assume the presence of bacteriophage or its anlage in every cell of the culture,i.e., it is part of the hereditary constitution of the strain.
Rough enteritids produces the phage although it will lyse inly smooth cultures of other organisms.

A mucoid resistant variant of the enteritidis to phage 13 was found to be lysogenic of 13 as well as for gallinarum. The mucoid strain was unstable and gave off rough and smooth colonies.

ib. Type differences amongst staphylococcal bacteriophages. 6:21-31. 4 phages found for a white coccus "SF". Some resistant variants were aureus pigmented, but nonpathogenic. (Among the phages was C-C'- see induced lysogenicity.)
/B is C-resistant.

Burnet 1932 JPB 35: 851

ABCD = phage types from BD (groups B and D)

A: lysis at margin, filled center — B: murky, sharper, uniform.

secd. uniform. — secd. heterogeneous

about 50% para B → A type only. — see Burnet 1930a JPB 33: 647

enteritidis → B most usually

typhimurium → A, D, N.

A + B are specific for smooth!
C is SR
D, N are SR or R. — gallinarum

rough strains may often produce S phages.

BTM strain (enteritidis) → phage S_1 (A phage) This is specific for smooth BD. (evidently no action on para A).

A phage from para A did not attack any ent sanguis and 1 enteritidis. (Is this true?) — role of I?

supports common origin of enteritidis, and para B with later divergence of somatic antigen (does not refer to enemas XII component).

Argues ecol. advantage of symbiosis

(over)

para C
highly path
for mouse!

suipestifer - Kunzendorf VI - VII

"European" suipestifer 5/8 lysogenic for smooth or rough sang.

other rarely lysogenic for suip., but detect in typhi suis.

typhi suis (F 12) best indicator.

para C ⇒ only FT2

most others (e.g. Thompson) also → second R phage

2 serological and resistance types: **H** (Kunzendorf) + suipestifer (**S**)

Range of action not clear e.g. interaction not stated

Burnet + Fresh (1936.) 14:27-38.

	x-resistance						Absorption by heat-killed cells	
Culture	A	B	C	c'	D	Au1	C	c'
SF	+	+	+	+	+	+	+++	++
SF/C	+	+	−	−	+	+	−	−
SF/c'	+	−	−	−	+	+	−	−

SF and SF/C are serologically identical, SF/c' distinct.

If SF is spread fairly heavily on dense C, no loss of colonies, but SF/C forms.

SF + stated C., then excess c'.

Explosive production of C grown on SF cultures, infected with a few particles Do. single bursts, 80-150 per burst, in 70-90 mins.

C' appeared in older cultures of SF/C, reaching a peak of 50%.

SF/C/Au1 remained lysogenic; SF/C could not be lysinfected by anti C serum. SF/C colonies were noted in the centre of C' plaques

SF/C/B did not liberate C' mutants.

Estimates 10-20% contents ~~to~~ became lysogenic.

See). d'Herelle, F + Rakieten, T.L. (1934) JID 54, 313.

Bruce White, P. (1937) Lysogenic strains of V. cholerae and the influence of lysozyme on cholera phage activity. J Path Bact 44:271-278.

Phage LL φ acts weakly on certain strains. Addition of lysozyme (egg white 1:25) enhances action to give more active filtrates.

LL-resistant strains of agglutinable V. cholerae (Bedsai) are generally lysogenic with it. Most existing lysates are therefore probably contaminated with it.

~~Thus~~ Chinese strains were sensitive, could be made lysogenic. El Tor and other vibrios ~~do~~ were emitted λ^+ or λ^s.

Once again, no lysis was seen with LL φ on Rough vibrio, but the phage multiplied and became lysogenic. "blockade immunity" interpretation:

J. Dorenbos

Fortin, L.B. (1945) A bacteriophage for Pseudomonas pyocyanea.
J Bact 50: 301-303.

Evans, A. C. (1940) The potency of nascent streptococcus bacteriophage B. J Bact 39: 597-604.

phage as released from lysing bacteria more active. Lysis?

(1942) Technique for the determination of the sensitivity of a strain of streptococcus to bacteriophage of type A, B, C, & D. J Bact 44: 207-209.

Phage enzymes

CRSB.

Lomniska 125:846 ~~126:~~ 127:962 128:379
129:151, 269 130:602, 144

$\phi \cdot X \cdot 174$ 138: 497

See also JPB 58:259

J Mol Biol 54:313

Proc Soc 48:359 (poem H ϕ)

Feldmeister, E. (1941) Z. Balet. (I), 147: 417-

d'Herelle, F. & Rabieter, T.L. (1934) J. I. D. 54: 313

Gratia, A. (1948) Lyse bactérienne par un filtrat bactériophagique sans multiplication des corpuscles. Ann IP 75: 472 - 484

C16 - lysis & plaque formation on pseudysenteriae Y6R

on coli 36, however, conc. phage causes a sterile area, but when spread, no plaques are formed, only a granular growth.

ℓ is not regenerated from coli 36 (Burnet). Do readily absorbed. (shown by heating mixtures to eliminate absorbed phage. Cells are lysed by microscopic examination in liquid medium.

Titre of C16 does not increase on coli 36, but does on dys-

Considers possibility of "lysin". Shows same behavior when grown on other hosts. ~~Host~~ bacteria do not lyse ~~co~~ coli 36. Phage antiserum inhibits lysis. Lytic agent is removed by absorption with sensitive Y6R. bacteria

Does not show numerical relationship of ℓ adsorbed to bacteria killed.

Gildemeister, E., & Ahlfeld, I. (1941) Beitrag zum Bakteriophagenproblem

Z. Bakt. (I) Orig., 147: 417-437.

Most intestinal contents carry phages (77% on dys., 7% on para B; 5% on S. typhi.) The latter are more often found in Salm. convalescents

---

Refers to earlier work Z B. 91:12 (1923)

" dass in den lysoresistenten Kulturen immer einige wenige lysosensible Keime vorhanden sind, welche zur Entwickelung von Phagen ausreichen. Experimentelle Beweise für diese Annahme sind jedoch bisher nicht erbracht worden." Many virgl. colonies of coli 88 tested.

Believes in growth without bacterial destruction. Disagrees.

Tested λ by filtration of suspensions.

32/50 (64%) of a variety of Salmonella strains tested were λ+, usually best for homologous types. E typhi, Para B, Breslau, para A, Gärtner)

11/30 (34%) of dys. tested were λ+ (SF, SY, Shiga, Flexner, usually for homologous type.

5/16 cholera λ+, specific for vibrio.

Coli λ usually active on dysentery.

Believes in activation of latent λ rather than infection & extrinsic λ. Opposes Bail's theory.

Classic cultures can be temporarily λ-.

d'Herelle, F., + Malcolm, T.L. (1934) J.I.D. 54:313-344.
Mutations as governing bacterial characters and serologic reactions.
also book.
Reduced lysogenicity. [See Malone, R.H., and Lahiri, M., Studies on Asiatic Cholera. Indian Medical Research Memoirs #14, Calcutta 1930: Theobald Spirilla S.

S. enteritidis, ATCC Danysz 404. stated to be λ⁻. Lysogenicity was induced by addition of a typhi ♀. Activity of λ became attenuated by daily transfer over several months. Some cultures became partially resistant, especially after 150 transfers. [i.e. not isolated?.

With λ₁+, λ₂ could be added.

Some of the symbiotic "mutant" are unstable.

Nicolle, P., Grabar, L., + Gibert, P. (1946) AIP 72: 814-88.

Fréquence de la lysogénécité et moindre fréquence apparente de la lysosensibilité parmi les bacilles paratyphiques B.

31 tested for λ on ~~3 + human dysentery indicators~~ strain 12, and to 1 + 9.

26 were λ+ (11%) With one exception, λ+ were resistant to λ_I, λ- were sensitive. The exception was marked very rough culture.

2 exceptions. λ from strain 1 and strain 9 shown to be different, serologically & in host range.

Bordet, J. + Bordet, P. (1946) Bactériophagie et variabilité microbienne. AIP 72: 161-173; 321-334.

S(λ-) → R(λ+), especially in ~~presence~~ absence of Ca.

"excès de calcium entrave l'apparition des type R producteur de principe".

Complete Ca deficiency (oxalate 20 drops 2.5%/5 ml). does prevents the change.

Tests for the λ involve heat heating culture. [May have been resorbed!]

See Hadley 1924 J.I.D. Pyocyanea λ]

Lisbonne's bact. at 37° has a metallic sheen, "glaieuse" at 10-12. cells encapsulated & metachromatic material "toluidine blue".

Change does not require Ca. Cold bacteria have not produced λ, reappears in 24 h. at 37.

Lisbonne ✓ indexes Shiga lysogenic. antiserum does not remove λ although pneumo is inhibited. lysis by λ is inhibited by oxalate, but cells are not decontaminated.

Write for strains].

Fish, Roy T. (1942) Studies on staphylococci. I. Occurrence of bacteriophage carriers among strains of Staphylococcus aureus. J. Inf. Dis. 71: 152-160.

Took a 4mm loopful overnight area of 1 x 6 cm. Spotted loopful lysate used in both directions; not always seen reciprocally. Incubated 5 h. at 31°, then at room temperature. Used zephiran 1:50,000 - 1:100,000 to sterilize lysates. [used milk agar for chromogenesis: 30 cc skim milk + 70 cc 1.5 % agar, mixed after autoclaving.]

With 45² combinations, 43 lysis was found.

No lysogenic combinations were found in coagulase-negative, albus strains. Ultimately found that 19/43 = 44% of coagulase positive strains carry λ. Considerable specificity found.
Reciprocal lysogenesis was not observed here. But sequences such as: 64 → 47 → 44 → 68 → 49
77

24 groups of λ noted. None active on albus.

5 frankly lytic cultures were found.

II. Identification of Staphylococcus aureus strains by means of bacteriophage. 71: 161-165.

showed that staph. from related cases gave same responses to a series of 27 & isolated as λ.

See Amer. J. Hyg. 40, 232-238 (1944) for III.

See Topley + Wilson 1936 p. 239

Thomas, R.C. (1948) Ohio J. Sci. 48(3):102-106. A method for removing transmissible lysins from secondary cultures of bacteria. (Ohio Agl Exp Sta - Wooster).

Exposure of lytic cells to nucleic acid from various sources gave colonies reacting with original lysins. Grew lysogenic (?) bacteria with 2/9 % NA in H_2O. R. temp 1-12 h. Poured plates and tested colonies.

Science 88:56-57 (1938). Transmissible lysins in water extracts of seeds.

Phytopath. 30: 602-611 (1940) Additional facts regarding bacteriophage lytic to Aplanobacter stewartii.

SB599
T5

Phage from resistant corn. Typical phages produce "transmissible lysins".

N K

McKie, M. (1934) The lysogenicity of coliform bacilli. A.J.E.B.M.S. 12: 169-175.

82 coliforms and 9 atypicals tested for lysogenicity by testing filtrates.

>31% gave phages in the primary filtrate, and in several cases there were two or more phages. (52 φ from 37 φ+). Rough Flexner VR dysentery was most susceptible (38 φ active). 13 were active on rough 398R gallinarum.

15/52 were weak and lost on passage
28 on Flexner VR
3 on coli KR, weak on Flx VR
3 on 398R, — on VR
3 specific S'φ on 398S; Shiga S and YS.

Complex cross-resistance

Dunbar, James M. (1948) Bacteriophage typing of untypable Salmonella typhi organisms. Nature 162:851. (Nov. 27)

Many cultures are contaminated with an "anti O" phage, rather "a type."

When [illegible] reduced, "agglutinations" are characteristic and ... types to I and IV [illegible] ... with specific Type II phage. Growth [illegible] serum was used to type these previously untypable strains.

These contaminated bacteria are "interfering with" type specific phages.

"Central Pathological Laboratory
M.E.L.F."

Taylor, H.E., (1949) Additive effects of certain transforming agents from some variants of pneumococcus. J. Exp. Med. 89:399-424.

Small scale (1500 ml) preparations of TP described. Bovine Serum Albumin as accessory factor.

Strains: A66 (SIII)
R36A (R) from D39 SII. Never reverts and readily transformed.
ER Extremely rough from R36A. Grows in aggregates.
SIII-1 ← SIII ←(A66 / TP) R36A.

SIII-2 " " .

ER can revert to R, especially in liquid medium. Stable in agarose shallow layer.
When SIII TP is added, R is regularly formed. BSA needed for regular effect.

RTP activity only from SIII and R36A bacteria. ER DNA and other NAs inactive.
In view of parallel ē S transformations, the ER → R effect is regarded as an induced change, not selection

anti R prevents ER → R. Thus it can be shown that ER ↛ S with SIII. "Like other morphological mutants obtained from R36A, ER is 'incompetent' to undergo direct transformation into the SIII condition.

ER → R → S was obtained in one tube by adding ~~3/4~~ anti R after S 3/4 h. and using SIII TP. ~~OR TP gene~~ R36A TP gave only R.

type-specific antisera inhibit transformation of R36A → STH N
but is essential for STH - 1

SIII-N (normal) - 1 and - 2 differ in amount of III substance.

anti III enzyme makes -1 and -2 cultures rough. ~~Does~~ Is less effective on III N.

III-1 requires very little antibody for agglutination. Does also agglutinated by R No quelling. Not mucoid.

III-2 mucoid, quelling but less III than III-N. Not virulent.

TP from III-1 and III-2 transform R36A to comparable S type. and ER to R.

Roughs obtained from III-1 and III-2 are transformable to III-N.

When mixtures of SIII-1 and SIII-2 are applied together, III-N bacteria were found as well as the -1 and -2 types.

$R \xrightarrow{1} III\text{-}1 \xrightarrow{N} III\text{-}N.$ Does not believe this goes through R as mediate.

$R \rightarrow III\text{-}2 \not\Rightarrow III\text{-}N.$

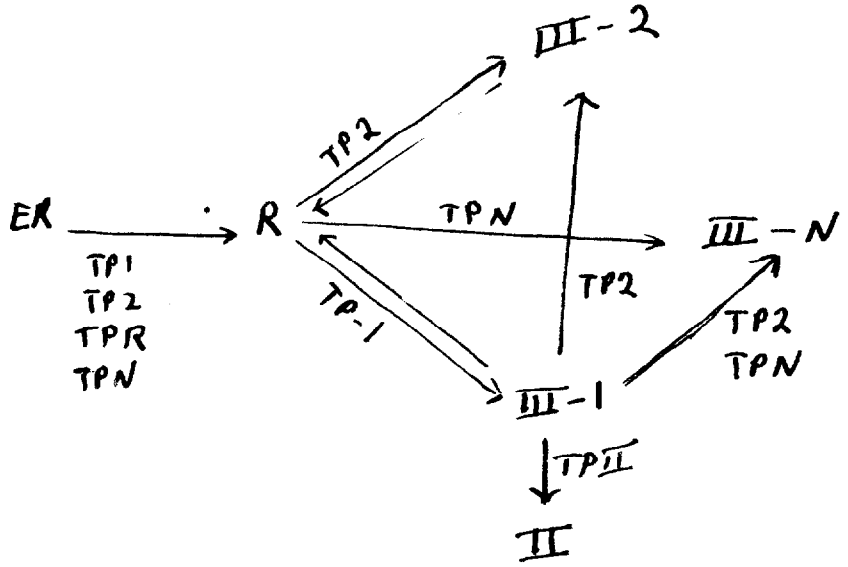
$R \rightarrow III\text{-}N \not\Rightarrow III\text{-}1$
$\not\Rightarrow III\text{-}2$

TP from SIII-N ($\leftarrow$ -1 $\leftarrow$ R) shows no signs of inducing SIII-1 from R. They show no signs of the intermediate stage.

$R \rightarrow III\text{-}1 \xrightarrow{\alpha} III\text{-}2.$ Summation may or may not take place
$\xrightarrow{TP\ III} III\text{-}N$

No statement whether the III-N type formed by summation is "heterozygous".

TP1
TP2
TPN
TPR



does not III-N from summation contain both transforming principles? [Evidence that interconversions do not go through R?]